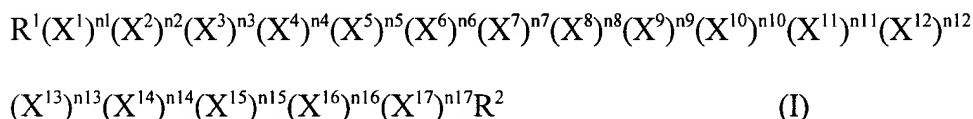


a.) Amendments to the Claims

1. (Currently Amended) A cyclic peptide, or a pharmaceutically acceptable salt thereof, having an activity to restore DNA-binding activity or P53 protein-dependent transcription activity to mutant P53 protein, said peptide being represented by formula (I):



wherein

any of X^1 to X^{17} may be denoted by X^i , i being an integer of 1 to 17;

any of $n1$ to $n17$ may be denoted by n_i , where n_i represents 0 or 1

such that $(X^i)^{n_i}$ represents X^i when n_i is 1 and represents a bond when n_i is 0;

n_i represents 1 for at least 7 different X^i 's;

any of X^1 to X^{11} where n_i represents 1 may be denoted by X^p , wherein p is 1-11 respectively, and any of X^8 to X^{17} where n_i represents 1 may be denoted by X^q where q is 8-17, respectively, such that $q > p$;

R^1 represents substituted or unsubstituted alkanoyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted aralkyloxycarbonyl, substituted or unsubstituted aryloxycarbonyl, substituted or unsubstituted aroyl, 9-fluorenylmethoxycarbonyl or hydrogen;

R^2 represents substituted or unsubstituted alkoxy, substituted or unsubstituted aralkyloxy, amino, substituted or unsubstituted alkylamino, substituted or unsubstituted dialkylamino, substituted or unsubstituted aralkylamino, substituted or

unsubstituted arylamino or hydroxy;

a functional group in X^p and a functional group in X^q together form a covalent bond to form a cyclic structure together with any intervening X^i residues;

X^1 represents a residue of 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptoputanoic acid, mercaptoacetic acid, adipic acid, suberic acid, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline or 4-hydroxyproline;

X^2 represents a residue of leucine, isoleucine, valine, alanine, norvaline, norleucine, 2-aminobutanoic acid, homoleucine, β -alanine, α -aminoisobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^3 represents a residue of lysine arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^4 represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-

mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X⁵ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁶ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁷ represents a residue of alanine, β -alanine, 2-aminobenzoic acid, 3-aminobenzoic acid, 4-aminobenzoic acid, 3-aminomethylbenzoic acid, proline, 3-hydroxyproline, 4-hydroxyproline, L-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid, cysteine, homocysteine, penicillamine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, ornithine, lysine, p-aminophenylalanine, aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid or glycine;

X⁸ represents a residue of glutamine, asparagine, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X⁹ represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-

aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹⁰ represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹¹ represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹² represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X¹³ represents a residue of histidine, alanine, 4-thiazolylalanine, 2-thienylalanine, 2-pyridylalanine, 3-pyridylalanine, 4-pyridylalanine, (3-N-methyl)piperidylalanine, 3-(2-quinoyl)alanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine,

aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X¹⁴ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid or glycine, and an amino group or guanidino group in the side chain of X¹⁴ may be modified with R³ (where R³ is independently selected from the moieties of R¹;

X¹⁵ represents lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X¹⁶ represents a residue of leucine, alanine, 4-thiazolylalanine, 2-thienylalanine, isoleucine, norleucine, homoleucine, valine, norvaline, β -alanine, α -aminoisobutanoic acid, 2-aminobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X¹⁷ represents a residue of 2-mercaptoaniline, cysteamine, homocysteamine, cysteine, homocysteine, penicillamine, ornithine, lysine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, p-aminophenylalanine, glutamic acid, aspartic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid or

2-aminosuberic acid;

where a 12-aminododecanoic acid residue may be added between R¹ and X^p nearest to the N-terminus, or between X^q nearest to the C-terminus and R², and the cyclic peptide does not comprise five or more consecutive glycine or lysine residues.

2. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 1, wherein said cyclic structure is formed by a S-S, S-CH₂-S, S-CH₂-C₆H₄-CH₂-S, S-CH₂-CO, CO-NH, NH-CO, O-CO or CO-O bond between X^p and X^q.

3. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^p (np=1) is an N-terminal residue and X^q (nq=1) is a C-terminal residue.

4. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^p (np=1) is not an N-terminal residue and X^q (nq=1) is not a C-terminal residue.

5. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^p (np=1) is not an N-terminal residue and X^q (nq=1) is a C-terminal residue.

6. (Previously Presented) A peptide or a pharmaceutically acceptable salt

thereof according to claim 2, wherein X^p ($np=1$) is an N-terminal residue and X^q ($nq=1$) is not a C-terminal residue.

7. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 3, wherein X^p ($np=1$) is X^1 and X^q ($nq=1$) is X^{17} .

8. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^p ($np=1$) is X^1 and X^q ($nq=1$) is X^{17} .

9. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 3, wherein X^p ($np=1$) is X^1 and X^q ($nq=1$) is X^{16} .

10. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^p ($np=1$) is an N-terminal residue and X^q ($nq=1$) is X^8 .

11. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 4, wherein X^p ($np=1$) is X^8 and X^q ($nq=1$) is X^{14} .

12. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 5, wherein X^p ($np=1$) is X^3 and X^q ($nq=1$) is a C-terminal residue.

13. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 4, wherein X^p ($n_p=1$) is X^3 and X^q ($n_q=1$) is not a C-terminal residue.

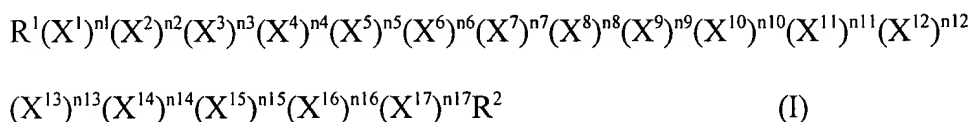
14. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^p ($n_p=1$) is an N-terminal residue and X^q ($n_q=1$) is X^{11} .

15. (Currently Amended) A peptide or a pharmaceutically acceptable salt thereof according to claim 1, said peptide having an amino acid sequence shown by one of ~~SEQ ID NOS: 4-7 and 16-32~~ SEQ ID NOS: 4, 6, 7, 16-20 and 22-32 in which a 12-aminododecanoic acid residue may be added between R^1 and X^p nearest to the N-terminus or between X^q nearest to the C-terminus and R^2 .

16. (Currently Amended) A peptide or a pharmaceutically acceptable salt thereof according to claim 15, said peptide having an amino acid sequence shown by one of ~~SEQ ID NOS: 4-7, 16, 19 and 25-32~~ SEQ ID NOS: 4, 6, 7, 16, 19 and 25-32 in which a 12-aminododecanoic acid residue may be substituted or added between R^1 and X^p nearest to the N-terminus or between X^q nearest to the C-terminus and R^2 .

17. (Currently Amended) A cyclic peptide, or a pharmaceutically acceptable salt thereof, having an activity to restore DNA-binding activity or P53 protein-

dependent transcription activity to mutant P53 protein, said peptide being represented by formula (I):



wherein

any of X^1 to X^{17} may be denoted by X^i , i being an integer of 1 to 17;

any of $n1$ to $n17$ may be denoted by n_i , where n_i represents 0 or 1;

such that $(X^i)^{n_i}$ represents X^i when n_i is 1 and represents a bond when n_i is 0;

n_i represents 1 for at least 7 different X^i 's;

any of X^1 to X^{11} where n_i represents 1 may be denoted by X^p where p is 1-11, respectively, and any of X^8 to X^{17} where n_i represents 1 may be denoted by X^q where q is 8-17, respectively, such that $q > p$;

R^1 represents substituted or unsubstituted alkanoyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted aralkyloxy carbonyl, substituted or unsubstituted aryloxy carbonyl, substituted or unsubstituted aroyl, 9-fluorenylmethoxycarbonyl or hydrogen;

R^2 represents substituted or unsubstituted alkoxy, substituted or unsubstituted aralkyloxy, amino, substituted or unsubstituted alkylamino, substituted or unsubstituted dialkylamino, substituted or unsubstituted aralkylamino, substituted or unsubstituted arylamino or ~~hydroxy~~, hydroxy, or

R^1 and R^2 together form a single bond;

X^1 represents a residue of 2-mercaptobenzoic acid, 3-

mercaptopropionic acid, 4-mercaptoputanoic acid, mercaptoacetic acid, adipic acid, suberic acid, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline or 4-hydroxyproline;

X^2 represents a residue of leucine, isoleucine, valine, alanine, norvaline, norleucine, 2-aminobutanoic acid, homoleucine, β -alanine, α -aminoisobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^3 represents a residue of lysine arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^4 represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptoputanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^5 represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁶ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁷ represents a residue of alanine, β -alanine, 2-aminobenzoic acid, 3-aminobenzoic acid, 4-aminobenzoic acid, 3-aminomethylbenzoic acid, proline, 3-hydroxyproline, 4-hydroxyproline, L-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid, cysteine, homocysteine, penicillamine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, ornithine, lysine, p-aminophenylalanine, aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid or glycine;

X⁸ represents a residue of glutamine, asparagine, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X⁹ represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹⁰ represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹¹ represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X¹² represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X¹³ represents a residue of histidine, alanine, 4-thiazolylalanine, 2-thienylalanine, 2-pyridylalanine, 3-pyridylalanine, 4-pyridylalanine, (3-N-methyl)piperidylalanine, 3-(2-quinoyl)alanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X¹⁴ represents a residue of lysine, arginine, ornithine, 2,4-

diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid or glycine, and an amino group or guanidino group in the side chain of X^{14} may be modified with R^3 (where R^3 is independently selected from the moieties of R^1 ;

X^{15} represents lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{16} represents a residue of leucine, alanine, 4-thiazolylalanine, 2-thienylalanine, isoleucine, norleucine, homoleucine, valine, norvaline, β -alanine, α -aminoisobutanoic acid, 2-aminobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^{17} represents a residue of 2-mercaptoaniline, cysteamine, homocysteamine, cysteine, homocysteine, penicillamine, ornithine, lysine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, p-aminophenylalanine, glutamic acid, aspartic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid or 2-aminosuberic acid;

where a 12-aminododecanoic acid residue may be added between R^1 and X^p nearest to the N-terminus, or between X^q nearest to the C-terminus and R^2 , the cyclic peptide does not comprise five or more consecutive glycine or lysine residues.

and the cyclic peptide cannot be formed by cyclizing the peptides

represented by any of SEQ ID NOS: 33-41:

~~SEQ ID NO: 33: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys~~
~~SEQ ID NO: 34: His Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser~~
~~Arg His~~
~~SEQ ID NO: 35: Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu~~
~~SEQ ID NO: 36: Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys~~
~~Lys Leu~~
~~SEQ ID NO: 37: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys~~
~~Gly Gln Ser Thr Ser Arg His Lys Lys~~
~~SEQ ID NO: 38: Ser His Leu Lys Ser Lys Lys Gly Gln Ser Thr~~
~~Ser Arg His Lys Lys Leu Met Phe Lys~~
~~SEQ ID NO: 39: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys~~
~~Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met~~
~~Phe Lys~~
~~SEQ ID NO: 40: Ser Arg Ala His Ser Ser His Leu Lys Ser Lys~~
~~Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu~~
~~Met Phe Lys~~
~~SEQ ID NO: 41: Gly Gly Ser Arg Ala His Ser Ser His Leu Lys~~
~~Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys~~
~~Lys Leu Met Phe Lys.~~